AMENDMENTS TO THE SPECIFICATION

IN THE SPECIFICATION:

Page 1

Please replace page 1 of the specification with the attached new Page 1 (amended sheet), located at the end of this Amendment.

Before line 1 of the specification, please insert the following new paragraph:

This Non-provisional application claims priority under 35 U.S.C. § 119(e) on U.S. Provisional Application No(s). 60/553,962 filed on March 18, 2004 and under 35 U.S.C. § 119(a) on Patent Application No(s). PA 2004 00454 filed in Denmark on March 22, 2004, the entire contents of which are hereby incorporated by reference.

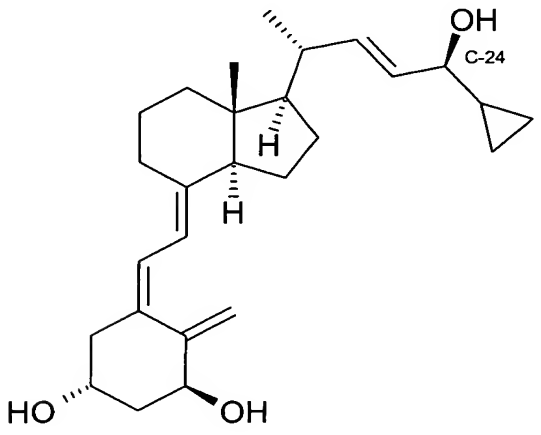
STEREOSELECTIVE SYNTHESIS OF VITAMIN D ANALOGUES

FIELD OF THE INVENTION

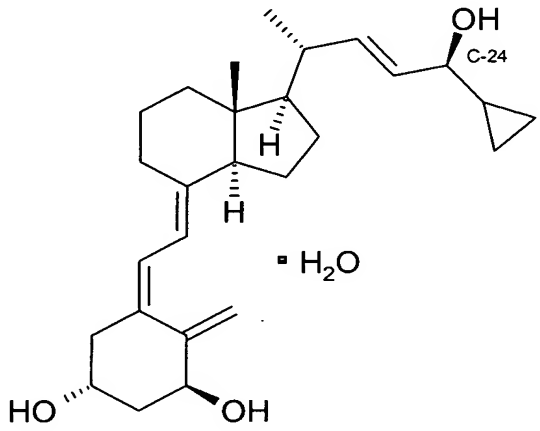
The present invention relates to methods of producing calcipotriol {(5Z, 7E, 22E, 24S)-24-cyclopropyl-9,10-secochola-5,7,10(19),22-tetraene-1α-3β-24-triol} or calcipotriol monohydrate by stereoselective reduction. The present invention further provides novel intermediates and methods for the synthesis of the intermediates useful for producing calcipotriol or calcipotriol monohydrate.

BACKGROUND OF THE INVENTION

Calcipotriol or calcipotriene (structure I) [CAS 112965-21-6] shows a strong activity in inhibiting undesirable proliferation of epidermal keratinocytes [F.A.C.M. Castelijins, M.J. Gerritsen, I.M.J.J. van Vlijmen-Willems, P.J. van Erp, P.C.M. van de Kerkhof; Acta Derm. Venereol. 79, 11, 1999]. The efficiency of calcipotriol and calcipotriol monohydrate (II) in the treatment of psoriasis was shown in a number of clinical trials [D.M. Ashcroft *et al.*; Brit. Med. J. 320, 963-67, 2000] and calcipotriol is currently used in several commercial drug formulations.



I



II

In the preparation of calcipotriol, the specific stereochemistry for the hydroxyl group at C-24 is necessary for full expression of the biological activity. Under current methodology, the required stereochemistry is introduced by one of the following methods: